Egyptian Herbal Monograph

Volume 2

Pharmacopoeial wild medicinal plants

Egyptian Drug Authority (EDA)

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***Datura stramonium* L.** داتورا

1. Names & Synonyms (1 - 4)

***Datura stramonium* L.**
Family: Solanaceae
Syns.: *Datura tatula* L.
Arabic: Datura داتورا , Tatura طاطورا.
English: Thorn-apple, Devil's apple, Jimson Weed, Stramonium.

2. Geographical distribution

Confined to Nile region (3).

3. Parts used for medicinal purpose

All parts possess medicinal value, though seeds and dried leaves with or without flowering tops are most widely used (2, 5-7).

4. Major chemical constituents

- **Tropane alkaloids**:
  - Hyoscyamine and hyoscine (scopolamine) (9).
  - 3-(hydroxyacetoxy) tropane, 3-hydroxy-6-(2-methylbutyryloxy)tropane, 3α-tigloyloxy-6-hydroxytropane, 3,7-dihydroxy-6-tigloyloxytropane, 3-tigloyloxy-6- propionyloxytropane, 3-phenylacetoxy-6,7-epoxytropane, 3-phenylacetoxy-6-hydroxytropane, aponorscopolamine, 3α,6 α -ditigloyloxytropane, 7-hydroxyhyoscyamine (10-14), 3-phenylacetoxy-6, 7-epoxynortropane, and 7-hydroxyapoatropine (15).
- **Steroids**:
  - Datura lactones (withanolides): withastramonolide (16), withatatulin and several others with anolides (17).
  - Ergostane-type sterols (18), stigmasterol and campesterol (19).
- **Essential oil:**
  Leaf oil: Phytol, diterpenes and oxygenated monoterpenes (9).
- **Other Constituents:**

Phenolic acids: Caffeic, *p*-coumaric, and ferulic acids; Flavonoids: chrysin, quercetin and their esters; Coumarins: umbelliferone, fraxetin, scopoletin, scopolin, umckalin; Amino acids: asparagines and glutamine; Fatty acids: daturic acid; Terpenes: hyoscyamilactol, daturaolone, daturadiol. *N-trans*-feruloyl tryptamine, tyramine, *N-trans*-ferulicacyl-tyramine; Coumarinolignoid: cleomiscosin A; Carbolines: 1-acetyl-7-hydrox-*β*-carboline and 7-hydroxy-*β*-carbolinel-propionic acid (19, 20); saponin and tannins (21).

5. Medicinal uses

A. Well-established (5)

- Spasmolytic
- Anti-asthmatic

B. Traditional use

- Rheumatic disease (7)

***D. stramonium* is a traditional medicinal plant for use in the specified indications exclusively based upon long-standing use.**

6. Herbal preparations correlated to medicinal use

1. Powdered herbal substances
   1.1 Leaves (7)
   1.2 Seeds (4).
2. Fluid extracts from leaves or seeds, tincture from leaves, powdered extract using the same amount of the stabilized standardized powdered drug (7).
3. Poultice (7).

7. Posology and method of administration correlated to medicinal use

Preparation 1
Indication A
1.1. A single dose of 50-100mg of stabilized powdered leaves (up to 3 times a day); maximum daily dose: 600mg in divided doses (4).
1.2. A single dose of 50mg of stabilized powdered seeds; maximum daily dose: 600mg in divided doses (4).

Preparation 2
Indication A
Equivalent to stabilized standardized powdered drug:

*Stabilized powdered leaves standardized to contain 0.23 to 0.27% of tropane alkaloids, calculated as hyoscyamine (22).
*Stabilized powdered seeds standardized to contain 0.4 to 0.6% of tropane alkaloids, calculated as hyoscyamine (4).

Preparation 3
Indication B
Leaves have been used as poultice (with some oil) for rheumatic pain (7).

Note: *D. stramonium* is to be dispensed by prescription only (a prescription drug). It is considered to be potentially harmful if not used under medical supervision.

Method of administration: Oral and topical use.

8. Contraindications

- Hypersensitivity to active substances and to other plants of the same family.
- Congestive heart failure; acute pulmonary edema; Constipation; Down syndrome; Seizures; Esophageal reflux; Fever; Stomach ulcer; Stomach and intestinal infections; Hiatal hernia; Glaucoma; Rapid heartbeat (tachycardia); Toxic megacolon; Ulcerative colitis; Obstructive digestive tract disorders (as atony, paralytic ileus, and stenosis); Urinary retention; Enlarged prostate (prostatic hypertrophy) (4); thyrotoxicosis; Asthma; Acute haemorrhage; hepatic disease; myocardial ischemia; CNS disorders (as myasthenia gravis); hyperthyroidism; hypertension; renal disease (23).

9. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- Children, patients with urine retention or coronary sclerosis should not use *D. stramonium* (4).
- Rubbing skin and eyes after contact with this plant is dangerous (2).

10. Interactions with other medicinal products and other forms of interaction

D. stramonium will have an additive effect when taken with other anticholinergic medications; co-administration of *D. stramonium* with other anticholinergic drugs may increase the frequency and/or severity of anticholinergic side effects (such as dry mouth, constipation, drowsiness, and others).

With drugs:

- *D. stramonium* will have an additive effect when taken with other anticholinergic drugs (drying medications) as atropine, scopolamine, some antihistamines and antidepressants; Together with these medications might cause side effects as dry skin, dizziness, low blood pressure, fast heartbeat, and other serious side effects. (4, 24).
- Antacids: decrease action of Jimsonweed (23).
- Phenothiazines: *D. stramonium* decreases the action of Phenothiazines (23).

With herbs:

Aloe, Buckthorn, Cascara, Chinese Rhubarb, Senna: *Stramonium* increase action in case of chronic use or abuse (23).

11. Fertility, pregnancy and lactation

- The use should be avoided during pregnancy and lactation as atropine component crosses the placenta and excreted in breast milk (23).
- *D. stramonium* may cause impotence (23).

12. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

13. Undesirable effects (23)

- If adverse reactions occur, a doctor or a pharmacist should be consulted
- **Central nervous:** Headache, dizziness, confusion, anxiety, flushing, drowsiness, insomnia, weakness, involuntary movements, decreased sweating, increased/decreased body temperature, coma, seizures, death (plant ingestion).
- **Cardiovascular:** Hypotension, paradoxical bradycardia, angina, premature ventricular contractions, hypertension, tachycardia, ectopic ventricular beats.
- Blurred vision, photophobia, eye pain, pupil dilatation, nasal congestion.
- **Gastrointestinal:** Nausea, vomiting, anorexia, dry mouth, abdominal pain, constipation, abdominal distention, altered taste.
- **Genitourinary:** retention, hesitancy, impotence, dysuria.
- **Integumentary:** hypersensitivity reactions, rash, urticaria, contact dermatitis, dry skin, flushing.

14. Overdose (4, 25)

- The intake of very high dosages leads to central excitation (restlessness, compulsive speech, hallucination, delirium, manic episodes), followed by exhaustion and sleep. The four early warning symptoms of poisoning are skin reddening, dryness of the mouth, tachycardia and mydriasis. Accommodation disorders, heat build-up through decline in sweat secretion, miction disorders and severe constipation can occur as side effects, particularly with overdosages.
- *D. stramonium* (in an oral dose of 1gm powdered leaves) acts as a narcotic.
- Lethal dosages (for adults starting at 100 mg atropine, depending upon atropine content, 15 to 100 g of the leaf drug, 15 to 25 g of the seeds, considerably less for children) carry with them the danger of asphyxiation.
- Treatment for poisoning include stomach emptying, temperature-lowering measures with wet cloths (no antipyretics), oxygen respiration for respiratory distress, intubation, parenteral physostigmine salts as antidote, diazepam for spasms and chlorpromazine for severe excitation.

15. Relevant biological activities

Antimicrobial effect

- The antimicrobial activity of *D. stramonium* (leaf ethanolic extract) was assessed against pathogenic bacteria. The plant showed significant antibacterial activity against the tested pathogens (26-29).

- Aerial parts (mainly stem and bark) of *D. stramonium's* aqueous and ethanolic extract were investigated for their antimicrobial effect on *Eschericia coli, Salmonella typhi, Staphylococcus aureus, Klebsiella pneumonia, Shigella and Neisseria gonorrhea*. The stem bark extract exhibited different inhibitory activities on the tested microorganisms. Ethanol extract exhibited the highest inhibitory activity against *K. pneumonia* followed by *S. aureus. S. typhi*. The aqueous extract showed activity only on *S. aureus*, while *N. gonorrhea* was resistant to both extracts (30).

- *D. stramonium* phytochemicals were investigated for their *in-vitro* activity against bacterial pathogens by disk diffusion method. *D. stramonium* leaf extracts exhibited a considerable antibacterial activity even at low concentrations. Of various fractions obtained from leaf, methanol extracts showed maximum inhibitory effect (31).

- The antibacterial activity was detected by agar well diffusion method against *Bacillus subtilis, Escherichia coli, Pseudomonas aeruginosa and Staphylococcus aureus.* The zones of inhibitions obtained were recorded and analyzed against standard control of Ampicillin. The methanolic extract showed higher antibacterial activity against *E. coli* and least antibacterial activity against *P. aeruginosa* (21).

- The plant extracts were tested on Gram negative bacteria *Escherichia coli* and on Gram positive bacteria *Staphylococcus aureus*. Both tested strains showed resistance but for *E. coli* a higher inhibition was observed at all samples containing *D. stramonium* extract (32).

- The antibacterial activity of aqueous extracts of different parts of *D. stramonium* (root, stem, leaf, seed and fruit coat) studied against five human pathogenic bacteria viz. *B. megaterium, B. cereus, E. coli, S. typhi and S. aureus*. The results indicated that aqueous extract of leaf were most effective against all the tested pathogens (33).

- The antimicrobial activities of *in-vitro* grown callus and *D. stramonium* methanolic extracts of root, stem, leaves, fruits, were studied against *E. coli, S. aureus and P. aeruginosa.* The methanolic leaf extract exhibited better antimicrobial activity against *S. aureus, E. coli, P. aeruginosa*. In the metabolite rich fraction (flavonoids, phytosterols and alkaloids), greatest bactericidal activity was exhibited by flavonoids against *P. aeruginosa* (34).

- The antibacterial activity of *D. stramonium* branches and leaves samples in three different solvents benzene, chloroform and ethanol was studied against *Enterobacter, Micrococcus luteus, Pseudomonas aeruginosa, E. coli, S. aureus and K. pneumonia*. All the solvent extracts showed significant antibacterial activity against tested pathogens. Comparative minimum inhibitory concentration of benzene, chloroform and ethanol extract determined that benzene extract was very effective against all bacterial strains (35).

- The methanolic extract of *D. stramonium* was screened for antimicrobial assay against different bacterial. Standard antibiotic (Azithromycin) and methanol were used as a positive and negative respectively. Leaf extract showed strong antimicrobial activity against bacterial species like *Bacillus thuringiensis, Pseudomonas aeruginosa, Agrobacterium tumefaciens and Klebsiella pneumoniae* (36).

-The fungicidal effects of the acetone extracts indicate the potential of *D. stramonium* seeds as natural source of antifungal agent. The MIC of *D. stramonium* extracts ranges from 1.25- 2.50mg/ml (37).

Antiasthmatic activity

- In 12 asthmatic patients with mild airway obstruction, the effect on specific airway resistance (sRaw) of inhaling the smoke of one *D. stramonium* cigarette was measured. In 11 patients sRaw decreased substantially after the cigarette, the mean maximal decrease being 40% at the 30th minute. Minor side effects were observed in six patients after the cigarette (38).

- The regular use of antiasthmatic cigarettes ever cannot be recommended for the following reasons: (1) the duration of action seems rather short. This could therefore lead to repeated inhalations and tachyphylaxis might occur. The risk of addiction from

overuse has also been suggested (2) the total composition of the smoke is not known. It may contain unwanted alkaloids, particles that may cause chronic mucosal inflammation, or even carcinogenic agents (38).

- The exposure of *D. stramonium* to the fetus when a mother uses it for asthma will cause a continuous release of acetylcholine, resulting in the desensitizing of nicotinic receptors, which could ultimately result in permanent damage to the fetus (39).

Anticholinergic activity

The alkaloids found in *D. stramonium*, are organic esters used clinically as anticholinergic agents. The anticholinergic syndrome results from the inhibition of central and peripheral muscarinic neurotransmission (40 - 43).

The antioxidant effect

- The antioxidant activity of methanolic extract of *D. stramonium* seeds was studied. The methanolic extract reduced the concentration of DPPH free radical with an efficacy near to that of standard antioxidant gallic acid, but less than butylated hydroxytoluene (BHT) (21).

- The methanolic extract of *D. stramonium* seeds is a potential source of natural antioxidants and significantly inhibit free radicals dose-dependently. The difference in the antioxidant activity may be ascribed to their different group of phenolic and flavonoid compounds. The extract showed higher phenolic content contributes to the higher antioxidant activity. Based on the results obtained, it can be concluded that the plant contains essential phytochemical constituents and possess antioxidant property (44).

Anticancer activities

- The evaluation of the cytotoxic effect of aqueous extract of *D. stramonium* leaves extract on different human cancer cell lines *in-vitro*. Breast (MDA-MB231), head, neck (FaDu), and lung (A549) cancer cell lines were treated with 1 mg/ mL of *D. stramonium* aqueous extract for 24 and 48 hours. The results may suggest therapeutic potential of *D. stramonium* aqueous leaf extract for the treatment of different types of cancer (45).

- *In-vitro* cytotoxic activity for breast cancer cell line (MCF7) was studied by MTT reagent assay method using the methanolic extract of *D. stramonium* seeds. The study do confirm that extracts exhibit cytotoxic effect on MCF-7 (44).

- Experiment on the cytotoxicity of methanol extracts of *D. stramonium* seeds on human breast adenocarcinoma cells (MCF-7) showed increasing cytotoxicity with increasing concentrations of extract and the viable cells detected by MTT assay (46).

Analgesic activity

The analgesic effect of alcoholic extract of *D. stramonium* seeds extract was evaluated in acute and chronic pain using hot plate and formalin tests. The extracts when administrated intraperitoneally administrated to the animals, the extract alleviated the pain dose dependently (ED_{50} values of 25 and 50mg/ kg in hot plate and formalin tests, respectively) (47).

Organophosphate poisoning

- *D. stramonium* contains atropine and other anticholinergic compounds, it is a useful remedy for the central cholinergic symptoms of organophosphate (OP) poisoning. The seeds were heated in water to make 2mg/ml atropine solution and administrated to male rats as a single intraperitoneal injection 5min before the subcutaneous injection of 25mg/kg of Dichlorvos . Pretreatment with *D. stramonium* seed extract significantly increased survival in a rat model of severe OP (48).

Antiepileptic effects

- According to Peredery and Persinger (2004), rats were continuously administrated once of three herbal treatments *S. lateriflora, G. sempervirens* and *D. stramonium* through water supply for 30 days, one week after the induction of status epilepticus by a single injection of lithium (3mEq/kg) and pilocarpine (30g/kg). The number of spontaneous seizures per day during a 15min observation interval was recorded for each rat during the treatment period and during an additional 30 days when only tap water was given. Rats that received a weak solution of the three herbal fluid extracts displayed no seizures during treatment. However, when this treatment was removed, the rats displayed numbers of spontaneous seizures comparable to the controls (49).

Anti-inflammatory activity

The ethanolic extract of *D. stramonium* leaves showed significant anti-inflammatory activity comparable to the standard drug Diclofenac sodium against carrageenan induced paw edema in rats. 39.43% inhibition of the edema was observed after 3 hours of oral administration of 200mg/kg extracts. Maximum activity was observed when the extract was administered in doses of 3-hours intervals (50).

Wound healing activity

The hydro-alcoholic extract of *D. stramonium* leaves was investigated for wound healing potential in rats. The leaves were dried, crushed and the hydro-alcoholic extract was obtained and turned to 10% ointment form. In the course of this study, 18 male wistar albino rats weighing approximately 150- 180g were used. Group 1 as negative control group, Group 2 as reference group were treated topically with Povidone-Iodine ointment USP, Group 3 as test control were treated with 10% *D. stramonium* ointment. Wound healing was monitored on days 4, 8, 12, 16 and

histopathological evaluation was carried out on the samples. Leaf extract of *D. stramonium* promotes wound healing via bactericidal activity (51).

Vibriocidal activity

Water, ethanol and acetone extracts of *D. stramonium* leaves were tested for their vibriocidal activity. A simple *in-vitro* screening assay was employed for the standard strain of *Vibrio cholerae*, 12 isolates of *Vibrio cholerae* non-O1, and *Vibrio parahaemolyticus*. The extracts were investigated by using the disk diffusion method. The results indicated that *D. stramonium* served as broad-spectrum vibriocidal agents (52).

Toxicity studies

- Due to *D. stramonium* anticholinergic activity, it has been reported as a drug of abuse and has been involved in the accidental poisoning of humans and animals. Symptoms of acute *D. stramonium* poisoning included dryness of the mouth and extreme thirst, dryness of the skin, pupil dilation and impaired vision, urinary retention, rapid heartbeat, confusion, restlessness, hallucinations, and loss of consciousness (53 - 55).

- Two doses of 50 and 200 mg/kg of the leaves ethanolic extract were administered to the rats for five weeks. Parameters studied were the indices of liver and kidney function and some biochemical and haematological parameters. Feed intake, final body weight, serum AST, ALT, billurubin, total protein, urea and the electrolyte studied were not affected by the extract administration. Serum creatinine levels were, however, significantly raised in the rats administered with the ethanolic extract at the dose of 200 mg/kg body weight. The biochemical and haematological parameters were also affected (56).

- Ingestion of *D. stramonium* seeds at concentrations of 0.5% or more in the diet have reported to produce adverse physiological changes in rats (57).

- The effects of acute, subacute and chronic administration of alkaloids atropine and scopolamine, the main active principle of *D. stromonium*, with toxic properties, were studied in male Albino Wistar rats. After acute *i.p.* administration of dose 100mg/kg of total alkaloids of the seeds of *D. stramonium*, there were no remarkable changes in general appearance and no deaths occurred in any experimental group. Twenty-four hours after administration of total alkaloids of seeds, a significant reduction in indices of liver, spleen, brain and kidney function and some biochemical and haematological parameters were observed. The red blood cells, hematocrit, hemoglobin and white blood cells were significantly higher in the treated groups than the control group. Subacute study for four weeks showed no resulting mortality or signs of toxicity. In chronic study, the synthetic alkaloids administered *i.p.* at daily doses of 4.2 mg/kg of atropine and 1.6 mg/kg of scopolamine, did not produce death. However, diarrhea and hypoactivity were observed. The relative weight of liver was significantly less than that of the control group (58).

Administration of scopolamine in drinking water to pregnant rabbits on days 10-14 of gestation led to fetal deformities of eye. These malformations were observed in all living fetuses present in six different animals (59).

-Various cases of toxic delirium and psychiatric symptoms have been reported after ingestion of *D. stramonium*. Careful consideration of the toxicity of the plant is required before its use. Its ingestion induces characteristic symptoms such as dry mouth, intense thirst, blurred vision, mydriasis and increased heart rate followed by hallucinations, delirium and loss of motor coordination leading to comma and ultimately to death by respiratory failure (55, 60 - 63).

16. Additional information

- Store *D. stramonium* in airtight containers. Protect from moisture and light (22).
- The atropine component is well absorbed, metabolized by the liver, and excreted by the kidneys (23).
- *D. stramonium* has also been smoked in cigarettes or burnt in powder and the fumes inhaled but the irritation produced by the fumes may aggravate bronchitis (22).
- Toxicity varies from season to season and depends on the manner in which the plant is ingested *i.e.* chewed, drank as an extract or smoked (64).

17. Date of compilation/last revision

30/8/2023.

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